IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF VIRGINIA
Alexandria Division

GEORGIA TORKIE-TORK,	)	
Plaintiff,	)	
	)	
v.	)	**No. 1:04cv945**
	)	
WYETH,	)	
Defendant.	)	

MEMORANDUM OPINION

In this removed diversity product liability action, plaintiff Georgia Torkie-Tork sues defendant Wyeth for compensatory and punitive damages, alleging that Prempro, a drug manufactured and sold by Wyeth, caused her to suffer breast cancer. At issue following discovery is whether summary judgment is appropriate in favor of Wyeth on plaintiff's claims for negligent design defect and fraud.[1] Wyeth argues that no genuine issue of material fact exists on either claim because, *inter alia*, (i) plaintiff has not adduced evidence of an alternative design for Prempro that would have avoided plaintiff's breast cancer, and (ii) the summary judgment record does not support a finding of fraud in the Prempro label.

For the reasons that follow, summary judgment in Wyeth's favor is appropriate with respect to part of the fraud claim, but summary judgment must be denied as to the remaining portion of the fraud claim and as to the claim for negligent design defect.

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[1] Wyeth moved for summary judgment on all claims except the claim for negligent failure to warn about the risks of breast cancer. Def. Br. at 1-2. Plaintiff conceded that summary judgment is appropriate on the claims for (i) strict liability for failure to warn, (ii) strict liability for design defect, (iii) negligent misrepresentation, and (iv) breach of express warranty. Pl. Br. at 16. Plaintiff opposes summary judgment on the two remaining claims, namely negligent design defect and fraud.

I.[2]

Plaintiff Georgia Torkie-Tork is a citizen of Virginia. Defendant Wyeth is a Delaware corporation with its principal place of business in New Jersey. During times relevant to this litigation, defendant was one of the world's largest pharmaceutical companies[3] and the maker of Prempro, a hormone therapy drug approved by the Food and Drug Administration ("FDA") that contains a combination of estrogen and a progestin ("E+P"), and is indicated for treatment of menopausal symptoms.

Beginning in or about 1996, plaintiff began experiencing severe menopausal symptoms. Her then-physician, Dr. Joel Schulman, prescribed Prempro for treatment of those symptoms. Between 1996 and 2002, several doctors filled out Prempro prescriptions for plaintiff, including Dr. William Hurwitz. Although he does not specifically remember prescribing Prempro for plaintiff, Dr. Hurwitz has stated that it is his general practice to read and rely upon the warning labels on any drug before prescribing it to a patient.

Between 1997 and 2002, the Prempro label contained the following statements:

> Some studies have reported a moderately increased risk of breast cancer (relative risk of 1.3 to 2.0) in those women on estrogen replacement therapy taking higher doses, or in those taking lower doses for prolonged periods of time, especially in excess of 10 years. The majority of studies, however, have not shown an association in women who have ever used estrogen replacement therapy. The effect of added progestins on the risk of breast cancer is unknown, although a moderately increased risk in taking combination estrogen/progestin therapy has been reported. Other studies have not shown this relationship. In a one-year clinical trial of PREMPRO, PREMPHASE and Premarin alone, 5 new cases of breast cancer were detected among 1377 women who received the combination treatments, while no new cases were detected among 347 women who received

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[2] The facts recited herein are derived from the pleadings and the record taken as a whole, and are not materially disputed except where specifically noted. Where such disputes are noted, the analysis proceeds by assuming plaintiff's claim of fact. *See Estate of Cloaninger v. McDevitt*, 555 F.3d 324, 332 (4th Cir. 2009) (citing *Scott v. Harris*, 550 U.S. 372, 377 (2007)).

[3] Pfizer Inc. purchased Wyeth at some point since the filing of this action.

> Premarin alone. The overall incidence of breast cancer in this clinical trial does not exceed that expected in the general population.
>
> . . .
>
> In the three year clinical Postmenopausal Estrogen Progestin Intervention (PEPI) trial of 875 women to assess differences among placebo, unopposed Premarin, and three different combination hormone therapy regimens, one (1) new case of breast caner was detected in the placebo group (n=174), one in the Premarin alone group (n=175), none in the continuous Premarin plus continuous medroxyprogesterone acetate group (n=174) and two (2) in the continuous Premarin plus cyclic medroxyprogesterone acetate group (n=174).

On August 7, 2000, the FDA wrote Wyeth to request that certain changes be made to the label for E+P hormone therapy drugs. *See* FDA Letter to Wyeth (Aug. 7, 2000). Specifically, the FDA's proposed changes included the following statements:

> While some epidemiologic studies suggest a very modest increase in breast cancer risk for estrogen alone users versus non-users, other studies have not shown any increased risk. The addition of progestin to estrogen may increase the risk for breast cancer over that noted in non-hormone users more significantly (by about 24-40%), although this is based solely on epidemiologic studies, and definitive conclusions await prospective controlled clinical trials.
>
> . . .
>
> Studies examining the risk of breast cancer among women using estrogen alone and combined estrogen/progestin therapy have suggested that there may be a mildly increased risk of breast cancer in women taking the combined therapy.

After receiving this letter, Wyeth's counsel responded to the FDA, noting that the FDA did not have the power to "dictate proposed language for an applicant labeling without providing a meaningful opportunity for dialogue between the applicant and the agency." Arnold & Porter Letter to FDA (Nov. 7, 2000). Wyeth also proposed alternative label revisions for the FDA's review with explanations for the areas of disagreement. Wyeth Letter to FDA (Aug. 11, 2000). For example, Wyeth stated:

> We strongly disagree with the presentation of the risk attributable to progestin use as 24-40%. First, we believe it is questionable for increases in risk to be stated only in percentages because this tends to exaggerate risk, particularly when

> absolute risk is small. Secondly, when stated only in this manner, the information is easily misinterpreted, i.e., one may interpret that 24-40% of all HRT users will develop breast cancer, a clearly inappropriate conclusion.

Wyeth then proposed the following alternative language:

> Epidemiological studies suggest that the addition of progestin to estrogen therapy may enhance [the risk of breast cancer over estrogen-only therapy]. Definitive conclusions await prospective controlled clinical trials.

This dialogue between the FDA and Wyeth concerning possible Prempro label changes continued until March 2001, at which time the FDA approved final revisions to the Prempro label. Pl. Ex. 25. Despite this approval in March 2001, Wyeth did not implement changes to its label until after a new study was released in July 2002 by the Women's Health Initiative ("WHI"). The WHI study showed a statistically significant link between the use of Prempro and breast cancer. Following the release of the WHI study, Wyeth updated the warnings on the Prempro label. Plaintiff alleges that the label on which her doctor relied when prescribing her Prempro was the pre-2002 version of the label, and Wyeth has conceded this reliance solely for the purposes of resolving the summary judgment motion.

The use of Prempro proved effective for the treatment of plaintiff's symptoms, and she continued using the drug until June 2002, at which time an abnormality was noted on her annual mammogram. At the direction of Dr. Ronald Orleans, she immediately discontinued her use of Prempro, and a follow-up sonogram and needle biopsy were performed. Based on the results of these procedures, plaintiff was diagnosed with breast cancer on June 18, 2002. Thereafter on June 27, 2002, she underwent a partial mastectomy to remove the cancerous tissue. A pathology report signed on July 3, 2002 confirmed that the cancer was hormone receptor positive, meaning that the cancer was of a type caused by hormones such as those contained in Prempro. A surgical procedure on July 24, 2002 confirmed that the June 27, 2002 mastectomy had removed all cancerous tissue. The cancer has not recurred.

Plaintiff filed the instant action in Virginia state court on July 2, 2004, and it was removed to this district on August 13, 2004. In her complaint, plaintiff alleges that Wyeth is liable for the personal injury that she suffered—namely, breast cancer—as a result of her prescribed use of Prempro. Because numerous suits of this nature had been filed, the Judicial Panel on Multidistrict Litigation convened multidistrict litigation ("MDL") proceedings in the Eastern District of Arkansas, and this matter was transferred to that district for participation in the MDL proceedings. *See Torkie-Tork v. Wyeth*, No. 1:04cv945 (E.D. Va. Nov. 1, 2004) (Conditional Transfer Order). At the conclusion of the MDL proceedings, by Order dated April 8, 2010, the matter was returned to this district for all further proceedings, including case-specific discovery, summary judgment, and if necessary, a trial. *See Torkie-Tork v. Wyeth*, No. 1:04cv945 (E.D. Va. Apr. 8, 2010) (Conditional Remand Order).

II.

The summary judgment standard is too well-settled to require elaboration here. In essence, summary judgment is appropriate under Rule 56, Fed. R. Civ. P., only where, on the basis of undisputed material facts, the moving party is entitled to judgment as a matter of law. *Celotex Corp. v. Catrett*, 477 U.S. 317, 322 (1986). Importantly, to defeat summary judgment the non-moving party may not rest upon a "mere scintilla" of evidence, but must set forth specific facts showing a genuine issue for trial. *Id.* at 324; *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 252 (1986). Thus, the party with the burden of proof on an issue cannot prevail at summary judgment on that issue unless that party adduces evidence that would be sufficient, if believed, to carry the burden of proof on that issue at trial. *See Celotex*, 477 U.S. at 322.

III.

Only two of plaintiff's claims are contested for the purposes of this summary judgment motion: (i) negligent design defect and (ii) fraud in the Prempro label.[4] Wyeth argues that plaintiff cannot establish certain elements of these claims and hence neither claim survives summary judgment. Additionally, Wyeth also argues that both claims fail for lack of evidence of causation.[5] Each of these arguments is addressed separately.

A. Negligent Design Defect

To prevail on a negligent design defect claim under Virginia law,[6] "the plaintiff must prove that the product contained a defect which [sic] rendered it unreasonably dangerous for ordinary or foreseeable use." *Alevromagiros v. Hechinger Co.*, 993 F.2d 417, 420 (4th Cir. 1993). Although not conclusive in determining what constitutes an unreasonably dangerous defect, "a court will consider safety standards promulgated by the government or the relevant industry, as well as the reasonable expectations of consumers." *Id.*

Wyeth contends that plaintiff's claim for negligent design defect fails for two reasons: (i) Prempro is "safe and effective" in light of the FDA's continued approval of the drug and doctors' continued prescription of the drug in its original form; and (ii) plaintiff has not adduced any evidence that an alternative design of Prempro, whether a variance in the dosage or an alternative formulation, would have avoided plaintiff's breast cancer.

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[4] *See* n.1 *supra*. At oral argument, plaintiff conceded that the only viable claim for fraud was fraud in the Prempro label.

[5] Wyeth further argues that all of the claims in plaintiff's complaint, including the claim for negligent failure to warn, should be dismissed for lack of causation.

[6] It has already been determined that Virginia law applies to this suit. *See Torkie-Tork v. Wyeth*, No. 1:04cv945 (E.D. Va. Jun. 16, 2010) (Mem. Op.).

As to Wyeth's first argument, plaintiff correctly notes, and Wyeth concedes, that FDA approval of a drug does not preempt an action for defective design. Pl. Br. at 17 (citing *Wyeth v. Levine*, — U.S. —, 129 S. Ct. 1187, 1204 (2009); *Hill v. Searle Labs*, 884 F.2d 1064, 1068 (8th Cir. 1989)); *see also* Def. Reply Br. at 19 ("Wyeth has never argued or implied that 'FDA approval is somehow sacrosanct' as to Plaintiff's design defect claim"). This is so because "FDA regulations are generally minimal standards of conduct" absent a clear intent by Congress to preempt state law, which has not occurred in this area. *See Hill*, 884 F.2d at 1068. Of course, the FDA's continued approval of Prempro in its current form is strong evidence of reasonableness in the Prempro design, and a jury may well conclude from this fact that Prempro's design is not defective. But this fact alone does not resolve the claim for the purposes of summary judgment.

Wyeth's second argument focuses on plaintiff's two alternative designs that would have decreased the risks of breast cancer for plaintiff and those using Prempro. The first proposed alternative design is simply a change in the dosage of the drug itself. The second proposed alternative design would have Wyeth use oral micronized (natural) progesterone instead of the synthetic progestin currently in Prempro.[7] Analysis of this argument must begin with consideration of the question whether the two proposed designs are in fact alternative designs for the purposes of the negligent design claim. Important in this regard is that an alternative design must not be an altogether essentially different product. As has been often stated, "[a] motorcycle could be made safer by adding two additional wheels and a cab, but then it is no longer a

[7] According to the Physician's Desk Reference, Prempro comes in several dosages, each of which contains a mixture of conjugated estrogens found in Premarin tablets—Premarin being derived from a mixture of sodium estrone sulfate and sodium equilin sulfate—and medroxyprogesterone acetate for oral administration. *Prempro*, Physician's Desk Reference (2010). The conjugated estrogens used in Premarin and Prempro are blended to match the average composition of material derived from pregnant mares' urine. *Id.*

motorcycle." *Caterpillar, Inc. v. Shears*, 911 S.W.2d 379, 385 (Tex. 1995); *see also Kimball v. RJ Reynolds Tobacco Co.*, 2006 U.S. Dist. LEXIS 27138 (W.D. Wash. Apr. 26, 2006) (noting that "'[t]wo-wheeledness' is an essential characteristic of a motorcycle"). Put another way, an alternative design is not reasonable if it alters a fundamental and necessary characteristic of the product. This is, of course, typically a question of fact, not law. *Kimball*, 2006 U.S. Dist. LEXIS 27138, at *8.

As to the first proposed alternative design, it may well be that the dosage of a drug is a fundamental characteristic of the drug, since a lower dosage may well alter or affect the positive impact the drug is designed to have on the human body. In her brief, plaintiff offers little explanation for the costs and benefits of a change in the dosage of Prempro, if such an analysis is even feasible with the current science available. Nevertheless, the decision properly rests with a jury to determine whether an alternative dosage of Prempro would so fundamentally alter the drug as to render it an entirely different product. Plaintiff's second proposed alternative design similarly presents an issue of fact properly submitted to a jury. If Wyeth could have used a natural progesterone instead of synthetic progestin and accomplished a similar positive therapeutic effect, a jury may reasonably decide that the refusal to employ such a design was negligent. On the other hand, Wyeth may martial evidence to show that this proposed alternative design would fundamentally alter Prempro, in which event a jury might reasonably conclude that such an alteration would result in a wholly different product—Prempro would no longer be Prempro, much as a four-wheel vehicle with a cab would cease to be a motorcycle. In short, on this issue—alternative design—the summary judgment record presents a genuine issue of fact for trial.

It remains then to resolve Wyeth's argument that plaintiff's proposed alternative designs would not have prevented plaintiff's breast cancer. Wyeth argues that plaintiff has only identified "generic experts" to discuss diminished cancer risks from plaintiff's alternative Prempro designs, rather than "case specific experts" who will show how the alternative designs would have avoided cancer in *this* plaintiff. Def. Reply. Br. at 17.

Wyeth's characterization of the experts as "generic" is misleading and unhelpful; plaintiff's expert reports indicate that alternative designs to Prempro would present little or no risk of breast cancer to *anyone*, which, of course, includes plaintiff. For example, Dr. Don Austin, one of plaintiff's expert witnesses, reviewed studies in this area and concluded "that [E+P hormone therapy] containing [natural] micronized progesterone or dydrogesterone has no elevated risk, in contrast to [E+P hormone therapy] containing [medroxyprogesterone acetate]," the synthetic form of progesterone. *See* Pl. Ex. 67, at 20, 27 (Report of Dr. Don Austin). Where an alternative drug design would nearly eliminate the overall risk of cancer, it follows *a fortiori* that it would also diminish that risk in the plaintiff's specific case. Wyeth may dispute Dr. Austin's conclusion, but viewing the record in a light most favorable to the plaintiff, which is appropriate at this stage, a genuine issue of material fact remains on the causation element of this claim. Accordingly, summary judgment is not appropriate for the negligent design defect claim.[8]

[8] This result is consistent with the decision in *Scroggin v. Wyeth* denying Wyeth summary judgment on the negligent design defect claims under Arkansas law. 2008 U.S. Dist. LEXIS 24027 (E.D. Ark. Jan. 14, 2008) (finding a genuine dispute of fact as to whether Prempro, "in the dosage consumed by Plaintiff, was in a defective condition and unreasonably dangerous"). On the other hand, the analysis in *Brockert v. Wyeth* is distinguishable from the present case. 287 S.W.3d 760, 769 (Tex. App. Ct. 2009). There, a state appellate court in Texas upheld the grant of summary judgment to Wyeth on a negligent design defect claim. The plaintiff in *Brockert* contended that the safer alternative design of Prempro would have been estrogen alone, and the Texas court recognized that such a design would essentially mean that "Prempro should have been a different product[,] [namely] its predecessor[,] Premarin." *Id.* at 769-71. Here, plaintiff argues that an alternative dosage formulation or a substitution of progestin with its natural

B. Fraud in the Label

It is well-settled in Virginia that two elements are essential to a fraud claim: (i) a knowing misrepresentation or concealment of material fact, and (ii) reasonable and detrimental reliance on that misrepresentation or concealment. *See Allen Realty Corp. v. Holbert*, 318 S.E.2d 592, 597 (Va. 1984); *Packard Norfolk, Inc. v. Miller*, 95 S.E.2d 207, 210 (Va. 1956). Plaintiff's fraud claim rests exclusively on the Prempro label, which plaintiff argues both misstates and conceals material facts about the cancer risks associated with Prempro.[9] To succeed on her fraudulent concealment allegation, plaintiff must show that Wyeth "conceal[ed] a fact that is material to the transaction, knowing that the [plaintiff or her doctors are] acting on the assumption that no such fact exists." *Clay v. Butler*, 112 S.E. 697, 700 (Va. 1922). Under such circumstances, "the concealment is as much a fraud as if the existence of the fact were expressly denied." *Id.*

The label contains four distinct statements, each of which must be separately analyzed for any potential fraudulent content.

i. Statement No. 1

> Some studies have reported a moderately increased risk of breast cancer (relative risk of 1.3 to 2.0) in those women on estrogen replacement therapy taking higher doses, or in those taking lower doses for prolonged periods of time, especially in excess of 10 years.

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counterpart would have been safer; whether such changes would fundamentally transform Prempro into a completely different product is a genuine issue of fact appropriate for jury resolution.

[9] At oral argument, plaintiff conceded that her fraud claim rests solely on allegedly fraudulent statements or concealments in the Prempro label, thus abandoning any other allegations of fraud contained in her complaint, such as fraud in Wyeth's marketing material. Although Wyeth disputes whether plaintiff's doctors actually relied on the label, Wyeth concedes that a genuine dispute of fact exists on the reliance issue, at least with respect to Dr. Hurwitz. As such, the central question in the summary judgment analysis of the fraud claim is whether the label included any fraudulent statements.

Plaintiff contends that this statement was fraudulent because, at the time the statement was made,[10] Wyeth knew that a risk of breast cancer existed for all doses of E+P, not just higher doses. But as Wyeth correctly points out, Statement No. 1 deals only with "estrogen replacement therapy," not E+P. The parties do not contest that "estrogen replacement therapy" is understood to mean estrogen-only therapy, and thus the term does not include estrogen-progestin (E+P) combination therapy. Furthermore, the parties do not dispute the truth of the statement with respect to estrogen-only therapy. Accordingly, Statement No. 1, by itself, was not fraudulent.

ii. Statement No. 2

> The majority of studies, however, have not shown an association [with breast cancer] in women who have ever used estrogen replacement therapy.

Plaintiff argues that Statement No. 2 was false at the time it was made because a majority of pre-WHI studies—32 out of 43—in fact showed a risk of breast cancer. Wyeth protests that plaintiff's tally of the studies is incorrect because it includes studies showing a statistically-nonsignificant increase in the risk of cancer from estrogen-related therapies. By defendant's count, only 18 of the 43 pre-WHI studies showed a statistically significant risk, making Statement No. 2 an accurate reflection of then-existing studies.

Defendant's emphasis on statistical significance is entirely appropriate. The concept of statistical significance is critical to a proper understanding of statistical analysis. Many studies provide their results in the form of a confidence interval, which is "a range of values calculated from the results of a study, within which the true value is likely to fall." Federal Judiciary

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[10] For the purposes of the summary judgment analysis, the statements on the Prempro label are evaluated for falsity during the period that plaintiff's physician allegedly relied on the label in prescribing the drug to plaintiff, namely the period from 1996 to mid-2002, just prior to the publication of the WHI study.

Center, *Reference Manual on Scientific Evidence* 360 (2d. ed. 2000). Confidence intervals are commonly used in epidemiological studies, and they must be carefully understood before drawing a conclusion from such studies.

The cancer studies cited by the parties typically report the correlation between a drug therapy and the incidence of breast cancer as a numerical relative risk; a relative risk greater than 1.0 generally indicates a positive correlation between the use of the drug and the incidence of cancer. Consider a study stating that the relative risk is 1.27, but where that value was contained in a 95% confidence interval bounded between 0.84 and 1.94. An equivalent way to state these results would be to say that there is a 95% probability that the relative risk value falls somewhere between 0.84 and 1.94. The range from 0.84 to 1.94 is called the confidence interval, and because of the nature of confidence intervals, the true value is no more likely to be at the low end of this range than at the high end. *Id.* at 361. Since a range of relative risk from 0.84 to 1.94 encompasses 1.0—the value at which there is no increase in the risk of cancer associated with the drug—then one must conclude that the results of the study are not statistically significant. Numbers like these are not hypothetical; indeed, these are the numbers taken from the 2002 epidemiological study by Dr. Stephen Hulley and published in the Journal of the American Medical Association—a study relied upon by plaintiff. *See* Hulley *et al.*, *Noncardiovascular Disease Outcomes During 6.8 Years of Hormone Therapy*, 288 JAMA 58, 60 (2002) (Pl. Ex. 71JJ). While plaintiff suggests that this study shows a risk of breast cancer associated with hormone therapy, defendant appropriately recognizes that the results of this study were inconclusive.[11]

[11] Statistical significance is a concept that is poorly understood in many contexts. For example, a political poll may show that one candidate leads another candidate in the polls 51% to 49%, but the fine print might note that the poll had a statistical error rate of plus-or-minus 2.5%. While

Of the 43 studies that the parties recognize as the universe of relevant pre-WHI cancer studies, plaintiff identified 32 studies that she believes showed a risk of breast cancer. Defendant contends that of these 32 studies, 14 do not show such a risk with statistical significance. Essentially, defendant claims that 14 of the studies cited by plaintiff either showed no risk of breast cancer or showed a relative risk of cancer within a confidence interval that includes 1.0, the latter of which would indicate an association that is not statistically significant. Each of these fifteen studies has been reviewed to verify defendant's claim, and the results of the studies are summarized in the table below:[12]

Pl. Ex. #	Author/Publication	Year	Statistical Results
Ex. 71G	Ewertz, Int'l J. Cancer	1988	RR 1.04 (95% CI 0.74-1.46) for pre-menopausal women; RR 1.16 (95% CI 0.64-2.11) for menopausal women; RR 1.28 (95% CI 0.96-1.71) for post-menopausal women; RR 1.04 (95% CI 0.69-1.57) for artificial menopause[13]
Ex. 9	Bergkvist, N. Engl. J. Med.	1989	RR 1.1 (95% CI 1.0-1.3) overall for estrogen users
Ex. 71H	Kaufman, Am. J. Epidem.	1991	RR 1.2 (95% CI 1.0-1.4) for estrogen unopposed by progestogens; RR 1.7 (95% CI 0.9-3.3) for estrogen opposed by progestogens
Ex. 71I	Colditz, Cancer Causes & Control	1992	RR 1.08 (95% CI 0.96-1.22) for ever-use of postmenopausal hormones

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some would assert that the poll shows one candidate to be leading the other by two percentage points, the only proper conclusion is that the candidates are in a statistical dead heat, because a 50-50 split is within the range of error. Arguments based on statistics must be evaluated carefully for such misleading statements.

[12] In reciting the results of the studies, the terms "relative risk" and "confidence interval" are abbreviated "RR" and "CI," respectively.

[13] These results reflect the risk of breast cancer associated with the use of non-contraceptive sex hormones in the respective groups. As the study summarized, "Exposure to [estrogen] or [progestogen], alone or in combination-type therapy, did not affect the breast cancer risk." Ewertz, 42 Int'l. J. Cancer at 835.

Pl. Ex. #	Author/Publication	Year	Statistical Results
Ex. 71M	Yang, Cancer Causes & Control	1992	RR 1.0 (95% CI 0.8-1.3) for ever-use of unopposed estrogen; RR 1.0 (95% CI 1.0-2.0) for current users
Ex. 71N	Weinstein, Int'l J. Epidem.	1993	RR 1.09 (95% CI 0.86-1.37) for ever-use of menopausal estrogen pills
Ex. 71P	Schairer, Cancer Causes & Control	1994	RR 1.0 (95% CI 0.9-1.2) for estrogen-only; RR 1.2 (95% CI 1.0-1.6) for estrogen and progestin
Ex. 71Q	La Vecchia, British J. Cancer	1995	RR 1.2 (95% CI 0.9-1.5) for ever-use of hormone replacement therapy
Ex. 71U	Levi, European J. of Cancer Prevention	1996	RR 1.3 (95% CI 0.9-1.9) for ever-use of hormone replacement therapy
Ex. 71V	Persson, Int'l J. Cancer	1997	Results for breast cancer association with estrogen replacement therapy not clear
Ex. 71X	Brinton, Menopause	1998	RR 0.9 (95% CI 0.7-1.2) for ever-use of hormone replacement therapy
Ex. 71JJ	Hulley, JAMA	2002	RR 1.27 (95% CI 0.84-1.94) for estrogen plus progestin therapy
Ex. 71KK	Kirsh, Cancer Causes & Control	2002	RR 1.14 (95% CI 0.81-1.59) for hormone replacement therapy
Ex. 71LL	Newcomb, Cancer Epidem., Biomarkers & Prevention	2002	RR 1.14 (95% CI 1.04-1.26) for ever-use of postmenopausal hormones; RR 1.28 (95% CI 1.16-1.43) for ever-use of postmenopausal hormones after adjusting for other observed factors

As the table indicates, one of the studies, the Persson (1997) study, did not provide its results in a form that facilitated straightforward analysis of the breast cancer risks from estrogen replacement therapy. Because the study lacks clarity as to its conclusions, it is appropriate to read the study in favor of plaintiff. Additionally, contrary to Wyeth's assertion, the Newcomb (2002) study apparently found a statistically significant association between hormone therapy and breast cancer. But even viewing the above 14 studies in a light most favorable to plaintiff, 12 studies do not show a statistically significant association between estrogen replacement therapy and breast cancer.

Removing these 12 studies from the 32 originally cited by plaintiff leaves just 20 pre-WHI studies that show a statistically significant risk of breast cancer. As previously stated, the parties agree that 43 studies constitute the proper universe of relevant, pre-WHI studies. Put another way then, 23 of 43 pre-WHI studies did not show a statistically significant association between breast cancer in women who have ever used estrogen replacement therapy. Accordingly, Statement No. 2 was not false.

iii. Statement No. 3

> In a one-year clinical trial of PREMPRO, PREMPHASE and Premarin alone, 5 new cases of breast cancer were detected among 1377 women who received the combination treatments, while no new cases were detected among 347 women who received Premarin alone. The overall incidence of breast cancer in this clinical trial does not exceed that expected in the general population.

Plaintiff argues that Statement No. 3 is false in two respects. First, plaintiff notes that although Statement No. 3 indicates that the study in question included 1,724 participants in all, almost one-fourth of the participants "dropped out" of the study. Pl. Br. at 12. Wyeth responds that dropouts in such studies are common, and in any event, that Statement No. 3 makes no representation about the participants who left the study. While the rate of participation in an epidemiological study may be appropriate to report along with the study's findings,[14] Wyeth did not act fraudulently in summarizing the study in question in Statement No. 3. An epidemiological study will include a multitude of factors that may affect the analysis and validity of, and confidence in, the results. Yet, including all of this information would have transformed the Prempro label into an extensive rehashing of the study's findings. The label is intended to provide a brief summary of the findings, and in this respect, the statement is reasonably worded

[14] For example, the Consolidated Standards of Reporting Trials Group recommends that such information be included in the "results" section of any randomized trial study. *See* CONSORT Statement § 13a (2010), *available at* http://www.consort-statement.org/consort-statement/13-19--results/item13a_participant-flow/ (last visited Sept. 22, 2010).

and not false. In light of the elevated standard of proof in a fraud claim, no reasonable jury could find fraud in this statement.

Plaintiff's second argument for fraud based on Statement No. 3 concerns the assertion that the "overall incidence of breast cancer in this clinical trial does not exceed that expected in the general population." Plaintiff contends that Wyeth knew this representation was false because an internal Wyeth document stated that the rate of breast cancer among study participants actually exceeded the rate of breast cancer among the population. But the internal document referenced by plaintiff clearly stated that the results of that study showed a standardized incidence ratio of 1.47 with a 95% confidence interval bounded between 0.47 and 3.43. Once again, plaintiff relies on the 1.47 value and ignores the fact that the confidence interval includes 1.0, making the results of this study statistically inconclusive. Accordingly, the summary judgment record does not support an allegation of fraud with respect to Statement No. 3.

iv. Statement No. 4

> In the three year clinical Postmenopausal Estrogen Progestin Intervention (PEPI) trial of 875 women to assess differences among placebo, unopposed Premarin, and three different combination hormone therapy regimens, one (1) new case of breast caner was detected in the placebo group (n=174), one in the Premarin alone group (n=175), none in the continuous Premarin plus continuous medroxyprogesterone acetate group (n=174) and two (2) in the continuous Premarin plus cyclic medroxyprogesterone acetate group (n=174).

Plaintiff argues that Statement No. 4 was "intended to deceive physicians and the public alike into believing that the PEPI trial was evidence that E+P does not causes [sic] breast cancer," even though "Wyeth knew all along that the PEPI trial told the world nothing about the breast cancer risk." Pl. Br. at 13. For her assertion about Wyeth's knowledge of the study's purpose, plaintiff relies on a Wyeth internal email recommending against including Statement No. 4 on the Prempro label because "PEPI was not designed to evaluate the risk or incidence of

breast cancer" in light of the small sample size of the treatment groups. *See* Email to Maida Burka (Jan. 10, 2001) (Pl. Ex. 55) ("January 10 Email").[15] This argument fails for two reasons. First, the suggestion in the January 10 Email was simply that "this information does not add any information to physicians or patients above our revised wording," not that the statement in the label was false. Pl. Ex. 55. *Id.* Second, Statement No. 4 specifically included the sample size (*i.e.*, "n=174") in its description of the study. Since the sample size was the basis for the January 10 Email's suggestion that the PEPI study was not designed to evaluate cancer risks, providing this sample size information on the label ensured that the study did not mislead doctors.[16] As such, neither the email nor the statement, standing alone, could lead a reasonable jury to conclude that Statement No. 4 is fraudulent.

Finally, in addition to alleging fraud in the statements on the Prempro label, plaintiff alleges that Wyeth acted fraudulently by excluding from the label the results of two additional studies in 2000. As recounted in Part I *supra*, in August 2000, the FDA requested that Wyeth change its Prempro label to include stronger statements about the risks of E+P hormone therapy. Wyeth and the FDA then corresponded for several months about alternative wording for these revisions before the FDA ultimately approved revisions in March 2001.

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[15] The email does not state, and the parties do not identify, the sender of the email, nor does the record explain the role of Maida Burka at Wyeth. Nevertheless, consistent with the obligation to view the evidence in a light most favorable to plaintiff, the sender and recipient are assumed to be experts with influential roles in advising Wyeth as to its drug labeling.

[16] One must assume for the purposes of this analysis that the doctor reading and relying upon the Prempro label had sufficient expertise to understand the significance of this information and evaluate the study's merits accordingly. If this were not true—that is, if a doctor who read this description of the PEPI study were unable to discern its meaning or significance—then the doctor would be unreasonable in relying on the information, and the fraud claim would fail for want of reasonable reliance.

At first glance, Wyeth's correspondence with the FDA would seem to belie any allegation of fraud. Wyeth carefully explained its concerns with the FDA's original draft of the revised warnings, and Wyeth ultimately reached an agreement with the FDA as to the appropriate changes to make. Had Wyeth implemented this agreed-upon revision, it would be very difficult for plaintiff to meet her elevated burden to show fraud by clear and convincing evidence. Yet, Wyeth did not actually implement changes to the label based on its discussion with the FDA. Indeed, changes were apparently not made to the 1997 Prempro label until after the 2002 WHI study. As such, Wyeth cannot rely on its negotiations with the FDA to justify its refusal to update its warnings between 2000 and 2002.

Wyeth argues that the fraudulent concealment claim nevertheless fails for two reasons: (i) plaintiff has not provided evidence of intent to commit fraud, and (ii) the scientific evidence in 2000 regarding the risks of E+P hormone therapy was inconclusive. As to Wyeth's first argument, it is well-settled that intent to deceive is most often proven by circumstantial evidence rather than "smoking gun" evidence. *See French v. Beville*, 62 S.E.2d 883, 889 (Va. 1951) (noting that "[f]raud is seldom, if ever, provable by direct testimony"). If plaintiff succeeds in showing that Wyeth knowingly concealed material information about risks of Prempro, then a reasonable jury might infer that Wyeth acted with the requisite fraudulent intent.

As to Wyeth's second argument, it is true of course that conflicting or inconclusive scientific studies may be a reasonable basis for Wyeth's refusal to include certain warnings on the Prempro label. Indeed, that argument lies at the heart of Wyeth's defense to the negligent failure to warn claim. Yet, as Wyeth concedes, a genuine dispute of fact exists on that issue. So, too, does such a genuine dispute of material fact exist with respect to this concealment in the label. While the fraud claim requires a higher showing of intent and a higher standard of proof

than the negligent failure to warn claim, the fraud claim is nevertheless bound up in a battle of the experts over whether the scientific evidence compelled changes to the Prempro label before 2002. Put succinctly, the summary judgment record, when viewed in a light most favorable to plaintiff, could lead a reasonable jury to find by clear and convincing evidence that Wyeth knowingly concealed information from the 2000 studies concerning the increased risk of breast cancer attributable to the use of drugs like Prempro. Accordingly, while summary judgment is appropriate for Wyeth on the allegations of fraudulent misrepresentation in the Prempro label, plaintiff's allegation of fraudulent concealment cannot be resolved on summary judgment.[17]

C. Causation

In addition to its specific attacks on plaintiff's fraud claims, Wyeth also argues that plaintiff has failed to prove causation in any of her claims because plaintiff's causation expert, Dr. Michael Wertheimer, bases his opinion on unreliable methods in violation of Rules 702 and 703, Fed. R. Evid., and *Daubert v. Merrell Dow Pharmaceuticals*, 509 U.S. 579 (1993). Wyeth has challenged Dr. Wertheimer's testimony in a separate *Daubert* motion that remains pending. While success on this motion may entitle Wyeth to summary judgment on plaintiff's remaining claims, that issue is not yet ripe for adjudication. Accordingly, the denial in part of summary judgment reflected in this Memorandum Opinion is without prejudice to Wyeth's right to file

[17] Wyeth argued that courts in other Prempro cases have granted Wyeth summary judgment on the fraud claim. Yet, cases cited by Wyeth in this regard are distinguishable. In *Rush v. Wyeth*, the plaintiff argued that Wyeth committed fraud in the promotion of Prempro's cardiovascular benefits. *See Rush v. Wyeth*, No. 4:03cv1507 (E.D. Ark. Dec. 14, 2006) (Order). By contrast, the present action alleges fraud in specific statements on the Prempro label, and omissions therefrom, concerning the risks of breast cancer associated with taking Prempro. And in *Bailey v. Wyeth*, the New Jersey state court found that the fraud claims were subsumed by New Jersey's statutory product liability laws. *See Bailey v. Wyeth*, No. MID-L-0999-06 MT (Sup. Ct. N.J. July 11, 2008) (Opinion). As such, these two cases are unpersuasive here.

another motion for summary judgment on the issue of causation should resolution of its *Daubert* motion warrant doing so.

IV.

Accordingly, summary judgment is appropriate in Wyeth's favor on the claim for fraudulent misrepresentation, but not for the claims of fraudulent concealment and negligent design defect. Additionally, summary judgment is appropriate in Wyeth's favor on the claims for strict liability for failure to warn, strict liability for design defect, negligent misrepresentation, and breach of express warranty, since plaintiff has conceded these claims.

An appropriate Order will issue.

Alexandria, Virginia
October 4, 2010

/s/
T. S. Ellis, III
United States District Judge